

## **Acanthosis Nigricans**

### **General:**

Acanthosis nigricans is a benign and common dermatologic condition consisting of velvety, hyperpigmented plaques on the skin. It most frequently occurs in intertriginous sites, but can occur anywhere on the skin or mucosa. Identification of acanthosis nigricans is important because it can be associated with a number of systemic abnormalities.

### **Epidemiology and risk factors:**

- Affects people of both sexes and all ages
- More common in African American, Hispanic, and Native American populations
- Particularly high prevalence in obese and diabetic people – present over 50% of African American and Hispanic children with DM2
- One study identified it in almost 20% of patients in primary care setting (including children)
- Vast majority of patients have
  - o Obesity – present in 51% of obese 7-19 yo pts, 37% of obese 20-39 yo pts
  - o Disorders associated with insulin resistance
    - DM2 – pts with acanthosis nigricans twice as likely to have DM2 (even after controlling for age, BMI), acanthosis nigricans present in up to 36% of newly diagnosed pts with DM2
    - Also present in patients with metabolic syndrome, PCOS, acromegaly, Cushing's syndrome
  - o Genetic syndromes, especially those associated with insulin resistance
    - Down syndrome, Rabson-Mendenhall syndrome (insulin receptor disorder), congenital generalized lipodystrophy, familial partial lipodystrophy
    - Consider genetic syndromes in patients with onset in early childhood
  - o Familial acanthosis nigricans that is not related to insulin resistance (rare)
  - o Malignancy – part of a paraneoplastic disorder, see below
  - o Drug reactions – systemic glucocorticoids, insulin, oral contraceptives, niacin, protease inhibitors, palifermin

### **Clinical manifestations:**

- Thickened, velvety or verrucous, brownish hyperpigmented plaques
  - o Initially skin can appear dirty, rough, and dry
  - o Later, there can be appearance of accentuated skin lines, wart-like projections, skin tags
- Most commonly in intertriginous sites (neck, axilla) or areas of skin folds, severe cases can involve other areas including mucosa (mucosal lesions generally are not hyperpigmented)
- Usually lesions are symmetrical
- Usually the lesions are asymptomatic, although they can have secondary infection

- Association with malignancy should be considered in certain situations:
  - o Older individuals that are not obese
  - o Rapid onset of lesions
  - o Additional paraneoplastic findings, including other dermatologic lesions like multiple skin tags or seborrheic keratoses
  - o Involvement of atypical sites (mucosa, palms/soles)
  - o Other symptoms suggestive of malignancy

### **Diagnosis:**

Usually clinical examination is sufficient. Biopsy demonstrates hyperkeratosis and epidermal papillomatosis. Inflammation is not a normal feature. Labs are helpful to identify associated conditions (DM, PCOS).

Important features of clinical examination:

- History – age of onset, symptoms suggestive of endocrinopathy, family history, exposures
- Physical exam – BMI, growth rate, signs suggestive of endocrinopathy

Consider malignancy-associated acanthosis nigricans in older, non-obese patients with new-onset acanthosis nigricans and no other identifiable cause. It is most commonly associated with gastric cancers (gastric adenocarcinoma 55% of malignancy-associated cases), but also with hepatocellular carcinoma and adenocarcinoma of lung, ovary, endometrium, kidney, pancreas, bladder, and breast.

### **Treatment and follow up:**

Treatment is generally for cosmetic concerns as it is a benign skin condition. Treatment should address the underlying causes, when possible. Improvement is not as likely in acanthosis nigricans associated with insulin-resistant states. Topical retinoids and vitamin D analogs may help. Scrubbing of the area should be discouraged as it can cause lichenification and worsening hyperpigmentation.

### **References:**

- Owen, C. Cutaneous manifestations of internal malignancy. In: UpToDate, Callen, J (Ed), UpToDate, 2012.
- Schwarzenberger, K. Acanthosis nigricans. In: UpToDate, Callen, J (Ed), UpToDate, 2012.
- Stulberg, D., Clark, N., & Tovey, D. (2003). Common hyperpigmentation disorders in adults: Part II. *American Family Physician*, 68(10), 1963-8.

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Hyperpigmented velvety plaques are present in the axilla.  
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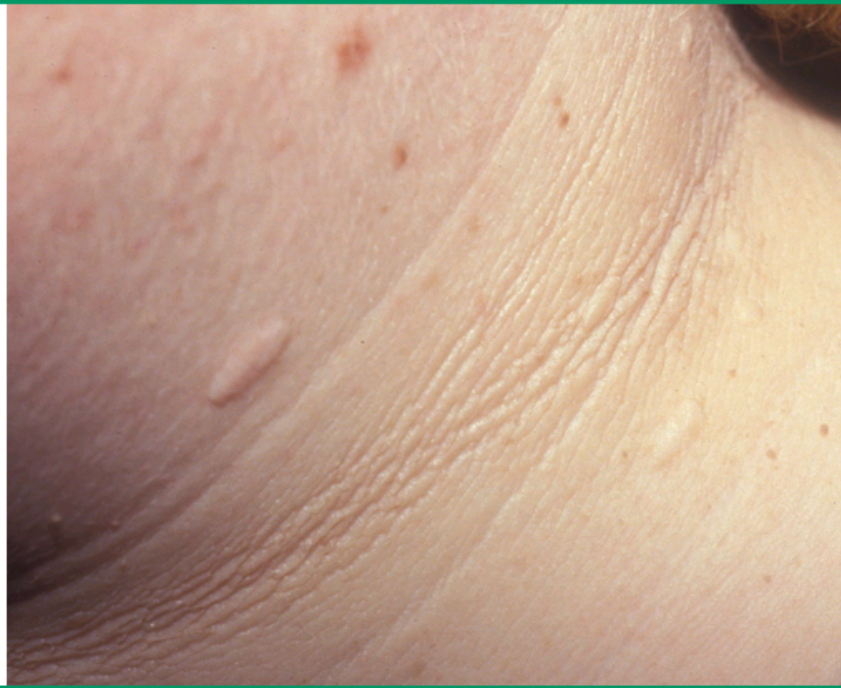
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Close view of acanthosis nigricans on the posterior neck.  
Hyperpigmented velvety plaques are present.  
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A velvety, slightly verrucous plaque is present on the neck.